Measurement Error in Nutritional Epidemiology: Impact, Current Practice for Analysis, and Opportunities for Improvement

Pamela Shaw

shawp@upenn.edu

on behalf of STRATOS TG4

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Perelman School of Medicine
University of Pennsylvania

Outline

- Background
- Motivating examples showing impact of Measurement error
- Regression calibration
- Literature survey: methodology and results
- Conclusions

STRATOS TG4: Measurement Error and Misclassification

MEMBERSHIP

- Laurence Freedman, Gertner/IMS , Co-Chair
- Victor Kipnis, NCI, Co-Chair
- Raymond Carroll, Texas A&M U
- Veronika Deffner, Munich, LMU
- Kevin Dodd, NCI
- Paul Gustafson, U. British Columbia
- Ruth Keogh, London School of Hygiene
- Helmut Kuechenhoff, Munich, LMU
- Pamela Shaw, U. Pennsylvania
- Janet Tooze, Wake Forest School of Medicine

TG4 Projects

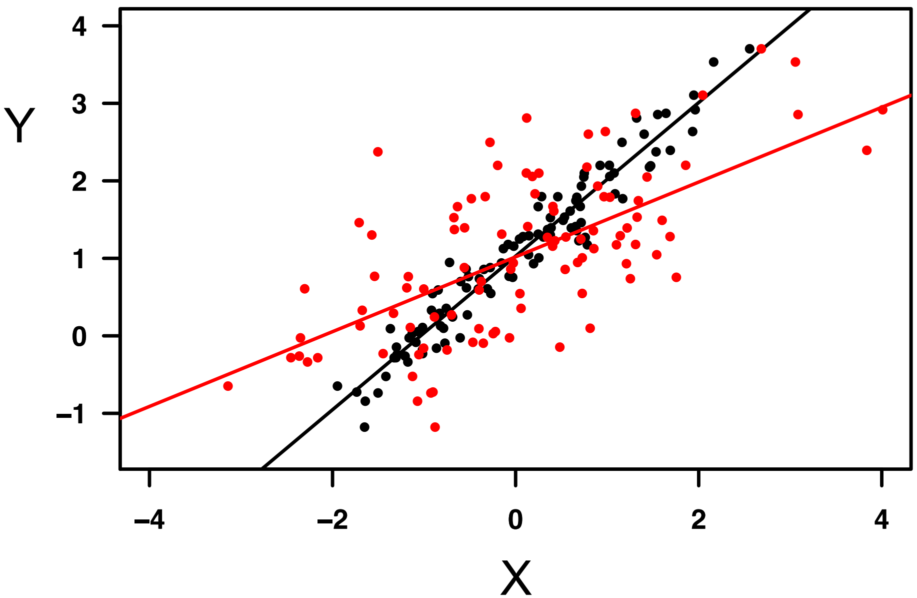
1. Literature Survey for how measurement error is addressed in 4 types of epidemiological studies
2. Guidance paper for nutritional epidemiologists
3. Guidance paper for biostatisticians

TG4 Literature Survey

- There have been many statistical advances to address in measurement error in the past few decades
- TG4 was interested in assessing the current practice for acknowledging and addressing measurement error in epidemiologic/observational studies
  - Want to identify knowledge gaps and opportunities for improvement
- We conducted a literature survey focused on types of epidemiologic studies with exposures that are well known to be subject to measurement error

Example1: Classical Measurement error

- Classical measurement error (CME) is random, mean zero error
- Covariate X* with CME can be written as: X* = X + u, where u is mean 0 error term independent of X and Y
- Suppose Y= β_0+ β_1 X + ε, then regressing Y on X* will estimate slope $\beta_1^* \neq \beta_1$
- β_1^* will be attenuated toward 0



$\boldsymbol{\beta_1^*} = \boldsymbol{\lambda\beta}$, where

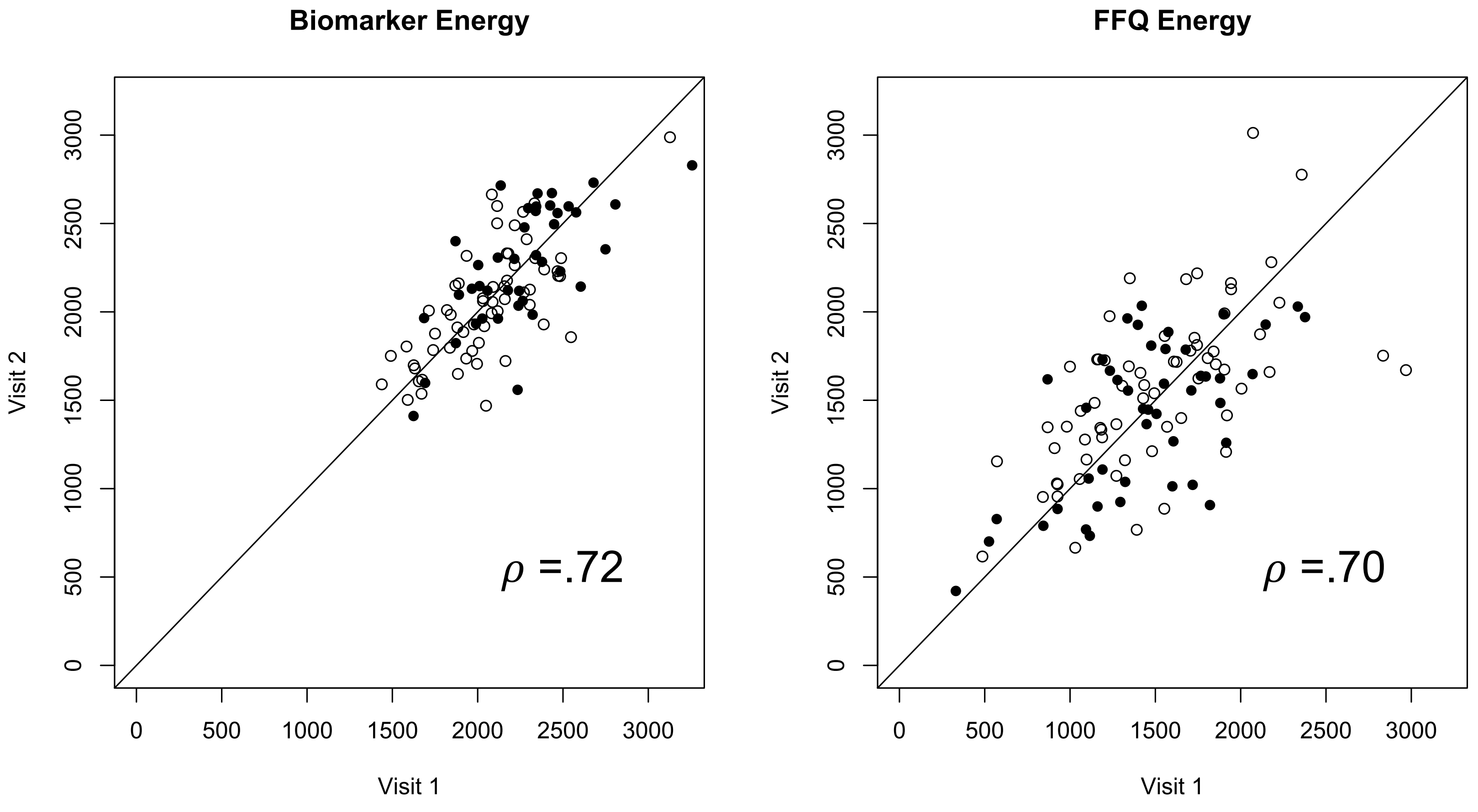
$$\lambda = \frac{\mathrm{var}(X)}{\mathrm{var}(X) + \mathrm{var}(u)}$$

So 0< λ <1

Example 2: Measuring Dietary Intake

- Measuring dietary intake is of interest in epidemiology as there are a number of diseases for which dietary factors are thought to be important risk factors, including cancer, heart disease and diabetes
- Dietary intake is a complex exposure to measure
  - Made up of many nutrients obtained from a variety of foods
  - Contains day-to-day variability, possibly also temporal variability
- There are several prevailing dietary assessment methods
  - Self-report: Food frequency questionnaire, 24hour recall, daily food record
  - Objective biomarkers: recovery or concentration markers

Measuring Energy Intake



Energy Intake vs Body Mass Index

Neuhouser et al AJE 2008

APPENDIX TABLE. Estimates of energy intake (kcal/day) obtained by self-reported food frequency questionnaire, a biomarker (total energy expenditure), and a calibrated food frequency questionnaire, according to body mass index category, Women's Health Initiative Nutritional Biomarkers Study, 2004–2005*

Body mass index† category	Self-reported FFQ‡		Total energy expenditure		Calibrated FFQ	
	Geometric mean	IQR‡	Geometric mean	IQR	Geometric mean	IQR
Normal (<25.0)	1,407	1,157–1,759	1,894	1,714–2,083	1,912	1,853–1,980
Overweight (25.0–29.9)	1,462	1,196–1,837	2,043	1,904–2,232	2,028	1,962–2,103
Obese (≥30)	1,454	1,161–1,897	2,213	2,034–2,415	2,247	2,156–2,338

* Note that the difference between FFQ energy intake (self-report) and total energy expenditure (biomarker) increases as body mass index increases. The biomarker-calibrated estimates, for the same women, correct for the measurement error using the model shown in table 4.

† Weight (kg)/height (m)^2.

‡ FFQ, food frequency questionnaire; IQR, interquartile range (25th–75th percentiles).

Regression Calibration: A simple approach to adjust for ME

Prentice Biometrika 1982

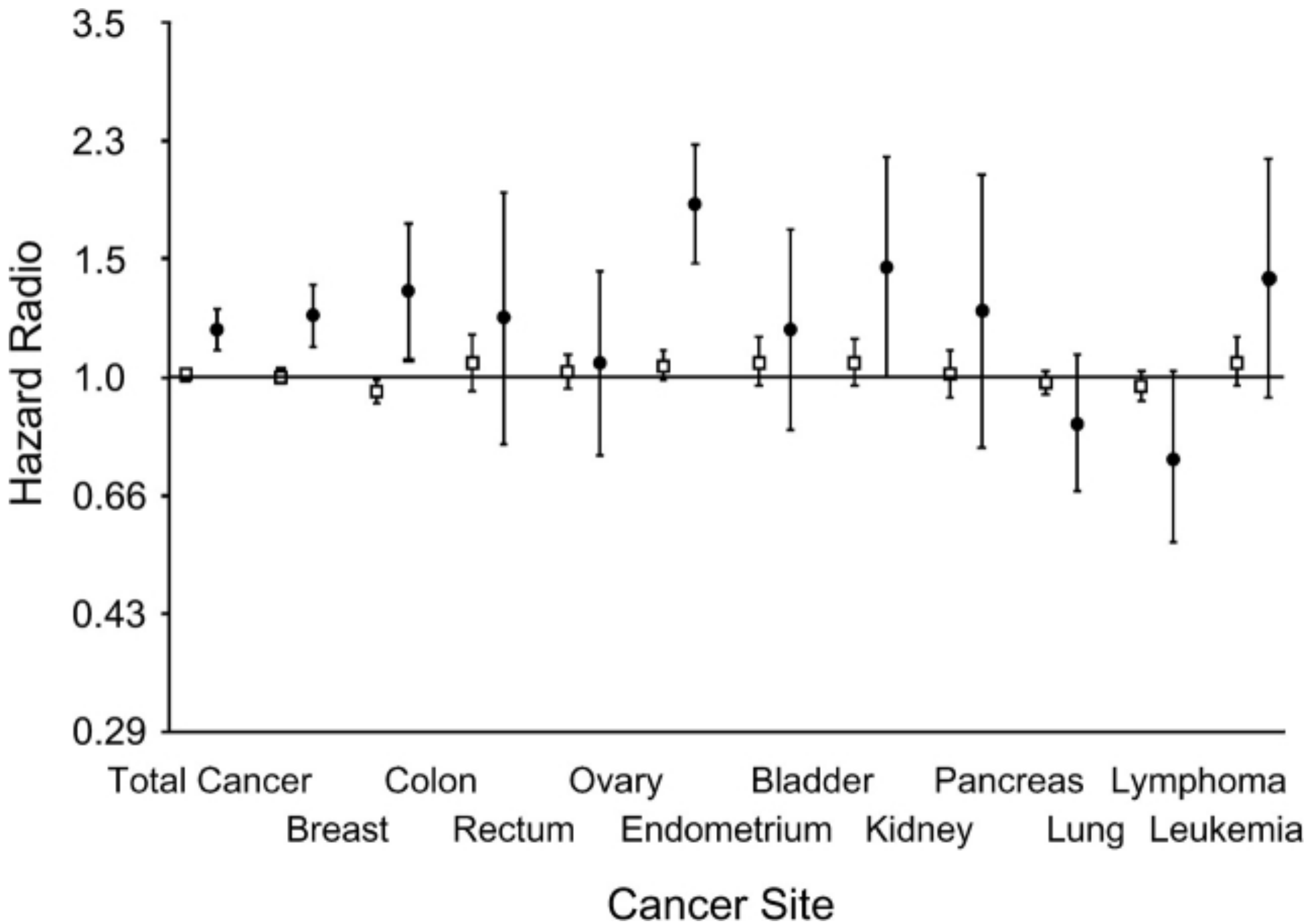
- Suppose true intake: X
- Error-prone measure: X* (FFQ intake)
- Objective biomarker: X** = X + u
- Predicted X = E(X**|X*,Z) = E(X+u|X*,Z) = E(X|X*,Z)

$$= a_1 + a_2 X^* + a_3 Z + a_4 Z X^*$$

Regression calibration: Regress outcome Y on predicted intake, other covariates Z

HR for Uncalibrated vs Calibrated Energy Intake

Prentice, Shaw et al AJE 2009



Survey Areas

Each of four topic areas had its own literature search

- Nutritional intake cohort studies (Pamela Shaw/Ruth Keogh)
- Dietary intake population surveys (Kevin Dodd)
- Physical activity cohort studies (Janet Tooze)
- Air pollution cohort studies (Veronika Deffner/Helmut Kuechenhoff)

Overall Approach

- Focused on error-prone variable as exposure in analysis
- For cohort studies, literature search done in two stages
  - <u>Search A:</u> Survey recent articles to assess how often articles acknowledged and/or addressed measurement error
  - <u>Search B:</u> Survey recent articles that adjusted for measurement error to describe methods in current practice
- Questionnaires filled out for each reviewed article
- Excluded reviews, cross-sectional studies, case-control studies and meta-analyses
- Each topic area conducted a quality control review
  - 20% re-reviewed by independent reviewer

Nutritional Epidemiology Cohort Studies: Survey Methodology

- Date Range A: Feb 2014-Jun 2015; B:Jan 2001-Jul 2015
- Limited search to three common diseases with dietary risk factors: cancer, heart disease and diabetes
  - Restricted date range to find about 50 articles from Search A and 30 articles from Search B
- Search B: added (measurement error OR misclassification to Search A
  - Not many articles, so did additional key word searches including: (measurement error OR misclassification) AND nutritional epidemiology
- Physical activity and pollution cohort methodology similar, except relied on date range and random sampling to reduce number of articles reviewed

Number of Articles Reviewed*

	Search A	Search B
Nutritional Epidemiology cohort studies	51	27
Dietary Intake Population Survey	67	N/A
Physical Activity cohort studies	30	40
Air Pollution cohort studies	50	25

* Number in table excludes articles that were identified by search terms but upon closer examination did not meet inclusion criteria

Search A Survey Results

	Nutritional Epi Cohort N= 51	Phys activity Cohort N=30	Diet Intake Survey N=67	Pollution Cohort N=50
Mention ME as potential problem n(%)	48 (94%)	17 (57%)	53/67 (79%)	20 (40%)
Used a method to adjust for ME N (%)	5 (10%)	0 (0%)	19/67 (28%)	3 (6%)
% categorizing exposure	Any 50/51(98%) Exclusively 27/51 (53%)	Primary exposure 21/30 (70%)		
Statistic of main interest N (%)	HR 45 (88%) OR 3 (6%) RR 2 (4%) Slope 5(10%)	HR 11 (37%) OR/RR 9(30%) GLM 5 (17%) Other 5 (17%)	Mean 51 (76%) Median 28(42%) %-tiles 21(31%) Quality 31(46%)	

Methods to Address Measurement Error

Nutritional Epi Cohort N= 27*	Phys Activity Cohort N=40	Dietary Intake Pop. Survey N=67	Pollution Cohort N = 25
Regression Calib. 26 (96%) SIMEX 1 (4%) Other 1 (4%)	Regression Calib. 1(50%) Other 1 (50%)	NCI 10(53%) Means 7(37%) ISU 1 (5%) MSM 1 (5%)	Sens Analysis 4 (80%) Instr Variables 1 (20%)
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Search A: None 90%	Search A: None 95%	Search A: None 72%	Search A: None 94%

- Number excludes articles that were identified by search terms but upon review did not use a method to correct for error.
- Row percents do not add to 100% due to use of multiple methods.

Other Observations from Diet and Physical Activity Cohort Surveys

- Common in the cohort studies to have multiple covariates with error: eg diet + physical activity, smoking, and/or alcohol intake
  - Many adjust for both diet+ PA, only 1 article adjusted for error in both physical activity (Zhang *et al*, AJE 2014)
  - Errors in smoking/alcohol not addressed
- Most categorized the continuous exposures
  - Impacts of categorizing an exposure subject to error are ignored
  - Common belief: categorization will lower impact of measurement error in the analysis
- Most people who mentioned error as a problem made an incomplete/incorrect claim
  - Many only mentioned attenuation in found associations
  - Some claimed no bias in associations since prospective subject recall
  - Some claimed no bias since instrument was validated

Other observations from Dietary Intake Population Surveys

- Most studies (80%) used 24HR as primary instrument
  - 31/53 used only 1 24HR, rest had repeats on at least a subsample
  - 8/31 (26%) reported percentiles subject to bias
- 16/31 papers with 1 24HR mentioned that usual intake or adjustment for within-person variation was needed
- 8/11 (73%) of papers using multiple 24HRs to report medians/percentiles, used a complex method (NCI/MSM)

Other Observations from the Air Pollution Cohort Survey

- Statements about the measurement error are often vague
  - The origin of the measurement error is often not clearly specified
  - The size and the impact of the measurement error is often not stated
- Measurement error is often mentioned but rarely addressed in detail or corrected
  - The majority of the studies use daily and spatially aggregated data
  - The often prevailing Berkson error (through temporal and spatial aggregation) is not or only insufficiently described and its implications are not discussed
  - Errors originating from staying in different microenvironments are often neglected or only poorly considered
- Many different exposure measures are analyzed separately or jointly; a homogeneous procedure is lacking

Conclusions

- In cohort studies: measurement error acknowledged, but implications not fully understood and commonly not addressed in statistical analysis
  - Very few used methods to adjust for measurement error
  - For PA studies, little motivation to adjust for error since the naïve associations are generally aligned with a priori hypotheses
  - Many studies had multiple variables measured w/error
- In dietary intake population surveys: minority corrected for measurement error
  - Majority of those that did apply a correction method were taking advantage of software (e.g. NCI method)
- Regression calibration most common method to address measurement error in diet and PA studies

More work is needed....

- Identify the various sources of measurement error
- Disseminate ideas of measurement error correction
  - Discussion of software in guidance documents, tutorials in clinical journals, talks at epi and clinical conferences
- Correct misconceptions, such as:
  - Random error won't cause bias in associations
  - Attenuation is the only possible direction of bias
  - Categorization reduces the effect of measurement error
  - Validated questionnaires don't have bias
  - Software is not available

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Regression Calibration

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Simex

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Multiple Source Method (MSM)

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NCI Method

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- Tooze JA, Kipnis V, Buckman DW, Carroll RJ, Freedman LS, Guenther PM, Krebs-Smith SM, Subar AF, Dodd KW. A mixed-effects model approach for estimating the distribution of usual intake of nutrients: the NCI method<image001.gif>. Stat Med 2010 Nov 30;29(27):2857-68.

Dietary Intake Population Studies: Survey Methodology

- Date range: Jan 2012 –May 2015
- Term “Measurement error” not typically referred to in dietary intake surveys
  - Understood as variance around usual intake
  - Conducted Search A only

Physical Activity Cohort Studies: Survey Methodology

- Date range: Jan 2012 – Sep 2015
- Search A: Very broad search terms: N=8760 from search; randomly selected N=610; N=51 from abstract review
- SEARCH B: Added "measurement error" OR misreport* OR misclassif* OR bias OR attenuat* OR calibrat*
  - N=610 from search; N=86 from abstract review

Air Pollution Cohort Studies: Survey Methodology

- Date range: Jan 2012 – Dec 2014
- Search A broad search within „Web of Science“:
  - Search B Additional keywords: "measurement error”, "measurement uncertainty”, misclassif*, attenuat*
  - A: 4595 hits, B: 386 hits
- After abstract review: A: 431 hits, B: 32 hits
- Random selection: Search A: 50/Search B:25